PATENT COOPERATION TREATY

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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P031663WO/CJM	FOR FURTHER ACTION	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/IB 03/04293	International filing date *(day/month/year)* 01.09.2003	Priority date *(day/month/year)* 30.08.2002
International Patent Classification (IPC) or both national classification and IPC A61K39/095		
Applicant CHIRON SRL et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 6 sheets, including this cover sheet.

   ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
30.03.2004	06.12.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Stoltner, A Telephone No. +49 89 2399-8408

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/IB 03/04293

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-15 as originally filed

Claims, Numbers

1-18 as originally filed

Drawings, Sheets

1/2-2/2 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

   These elements were available or furnished to this Authority in the following language: , which is:

   ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).

   ☐ the language of publication of the international application (under Rule 48.3(b)).

   ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

   ☐ contained in the international application in written form.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority in written form.

   ☐ furnished subsequently to this Authority in computer readable form.

   ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

   ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

   ☐ the description, pages:

   ☐ the claims, Nos.:

   ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 17

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 17 (relative to a method of treatment)

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

   ☐ the written form has not been furnished or does not comply with the Standard.

   ☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	
	No:	Claims	1-18
Inventive step (IS)	Yes:	Claims	
	No:	Claims	1-18
Industrial applicability (IA)	Yes:	Claims	1-18 (except claim 17 for some contracting states within the PCT)
	No:	Claims	

2. Citations and explanations

see separate sheet

ad section V:

1). The present application concerns the manufacture of an outer membrane vesicle (OMV) from a bacterium, wherein the bacterial membrane is disrupted "substantially" in the **absence of deoxycholate detergent** (claims 1-12), a composition containing the OMV resulting from the manufacture according to the preceding claims (13-15), and finally the use of such a composition in therapy (claims 16-18).
The problem to be solved resides in the provision of OMVs which are obtained in the **absence of detergent** normally necessary in the process of bacterial membrane disruption during the manufacture procedure, thus resulting in the obtention of improved bacterial immunogenic components.

2). The following documents will be discussed with reference to the subject-matter of the present application:

D1, WO-A-02/062378, relates to gram-negative bacterial strains with improved outer-membrane vesicle (OMV, also referred to as "bleb") shedding properties (cf. abstract, page 2, 1st para., claim 2). On page 10 (2nd para.), the manufacture of such blebs is explicitly said to be made **without the use of detergents** such as deoxycholate. Methods for the manufacture of OMV by using the basic steps according to claim 1 as presently on file are common prior art knowledge (cf. page 24, lines 15-25, page 26, lines 9-18). The subject-matter of claims 1-3 as presently on file has to be considered as anticipated with regard to D1.

D2, WO-A-01/91788, provides a vaccine including OMV from Neisseria (cf. abstract, page 6, 2nd and 3rd paras.). On page 7, D2 refers in a general way to the proceedings of manufacturing OMV expressly recurring to the use of deoxycholate (DOC) in the extraction of bacterial mass. D2 as such has no relevance to the presently claimed subject-matter which is directed to the manufacture of OMV in the **absence** of DOC.

D3, US-A-2002/0110569, provides vaccines comprising OMV for the prevention of diseases caused by Neisseria bacteria (cf. abstract, page 3, features [0019] and [0028], page 6, feature [0068]). On page 8, feature [0091], D3 explicitly stresses the detergent extraction step in the presence of a detergent other than DOC. This apparently falls into the scope of claim 1 as presently on file.

3). With regard to the documents cited above, the manufacture of OMV (and the resulting products thereof) in the absence of DOC or in the absence of any other detergent clearly arises from the teaching of D1 (cf. page 26, 3rd para.) and D3 (cf. page 18, feature [0185]).
The present application therefore fails to comply with the requirements of novelty and inventive step pursuant to Arts. 33(2) and 33(3) PCT.

4). For the assessment of the present claim 17 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

4a) Corresponding passages throughout the description referring to a method of treatment (cf. e.g. page 9) are to be removed or so redrafted as to indicate a possible application of the invention.

5). Incorporations made by reference (cf. page 1) are not accepted in the working practice of the EPO.

6). General statements in the description trying to extend the scope of protection to be sought in an ambiguous way (cf. page 4, line 26, "..not limited to..", page 11, last para.) are to be removed from the application.